Development of RNA-based approaches to stem cell gene therapy for HIV

Grant Award Details

Development of RNA-based approaches to stem cell gene therapy for HIV

Grant Type: Early Translational II

Grant Number: TR2-01771

Project Objective: Goal of the project is to develop RNA-based cell and gene therapy for HIV.

Investigator:

Name:	David DiGiusto
Institution:	City of Hope, Beckman Research Institute
Type:	PI

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Name:	John Rossi
Institution:	City of Hope, Beckman Research Institute
Type:	Co-PI

Disease Focus: HIV/AIDS, Immune Disease

Human Stem Cell Use: Adult Stem Cell

Cell Line Generation: Adult Stem Cell

Award Value: $3,097,160

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4/NCE

View Report

Grant Application Details

Application Title: Development of RNA-based approaches to stem cell gene therapy for HIV

Public Abstract: Despite significant advances in treatment and prevention programs, HIV infection with progression to Acquired Immunodeficiency Syndrome (AIDS) is still prevalent in California. The CDC Estimates >56,000 new cases of HIV infection each year in the US with over 148,000 cumulative cases reported in California alone (as of 2009). Multi-drug therapy has been helpful in reducing the severity of disease and prolonging lifespan but sixteen of every one hundred HIV patients will eventually fail to control the virus after attempting at least 2 drug treatment regimens. The Centers for Disease Control (CDC) recently estimated the lifetime cost of medical care for AIDS to be in excess of $600,000 per patient, over 85% of which is attributable to prescription drug costs. Additionally, medication non-compliance, intolerance of drugs due to side effects and the development of resistant strains of virus are all complicating factors in obtaining consistent clinical benefit with lifelong drug therapy. Therefore, there is a need to provide a longer lasting, cost effective therapy for this disease. Our project builds on prior work from our laboratories in which genetically engineered blood stem cells were transplanted into HIV patients and shown to give rise to gene-marked peripheral blood cells that last for up to 2 years. These cells may protect HIV patients from progression to AIDS if they are present in sufficient numbers. Our therapeutic candidate is a gene modified human blood stem cell carrying multiple anti-HIV molecules that prevent virus infection, replication and spread and a gene that allows us to chemically “enrich” the number of disease resistant cells present in a patient’s blood. The anti-HIV molecules are made of ribonucleic acid (RNA) and were developed and tested in our laboratories. We have already conducted a first generation stem cell therapy clinical trial to test these molecules with promising results. We now propose to refine and further develop this treatment with second generation RNA molecules and gene transfer procedures that will improve the number of disease resistant cells in the blood of HIV patients. We will develop an animal model system to test newer, more efficient anti-HIV molecules and a drug treatment method to enhance the number of HIV resistant stem cells circulating in the blood of patients that receive gene modified blood stem cells. At the end of the proposed experiments, we expect to have selected the most efficient combination of RNA molecules and drug selection strategy to provide a sufficient number of disease resistant cells in the peripheral blood to prevent progression to clinical immunodeficiency (AIDS).

Statement of Benefit to California:	California has ~14% of all cases of AIDS in the U.S., and this translates into a medical and fiscal burden larger than any other state except NY. Antiviral chemotherapy accounts for approximately 85% of AIDS-related medical costs, and federal and state law requires that in California the AIDS Drug Assistance Program (ADAP) be the payer of last resort for these medications. Antiretroviral drugs currently cost about $12,000 per year and account for about $350 million of the California AIDS Drug Assistance Plan's budget. The Governor's spending plan (2009-09 Budget Act) called for $418M to support this program, with funds from several sources including federal (Ryan White Care Act), from an ADAP Rebate Fund, and from the California State General Fund. The ADAP Rebate Fund consists of monies paid to the state by the manufacturers of the drugs provided to the HIV/AIDS clients under the program. The ADAP budget has grown by ~15% yearly for several years, and based on an Legislative Analyst's Office (LAO) review, the problem faced is that, as the case load is increasing, support from the Rebate Fund is decreasing. It is projected by LAO that from a level of $80.3 million at end 2008, the Fund will decrease to $24M by the end of 2010. The General Fund currently provides $96.3M to the ADAP budget, and it is projected that as the ADAP Rebate Fund shrinks, the shortfall will have to be met by increases from the General Fund by 2012. The alternative, as noted by LOA, is to implement cost-cutting measures that would likely increase the barriers to receiving care for some patients, impacting the health of some HIV/AIDS patients and increasing the associated public health risks.

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